

Application No. 09/977,880

Attorney Docket No: 58172-8004
Client Docket No. P1999002US-101RECEIVED
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REMARKS

Reconsideration of the claims submitted herein and withdrawal of the outstanding rejections in the instant application as set forth in the Office action mailed July 31, 2006 are respectfully requested in view of the amendments and arguments presented herein.

I. Status of the Claims

Claims 1-6 and 9-30 are pending in the application.

Claims 7 and 8 have been canceled.

Claims 1-5, 9, 11-22 are currently amended.

Claim 6 is as previously presented.

Claim 10 is original.

Claims 23-30 are new.

II. Amendments to the Claims

Claims 1 and 22 have been amended to conform to U.S. spelling practice, and to more clearly reflect the features of the claimed process for preparing a polymerizable composition. Specifically, claims 1 and 22 have been amended to more clearly recite formation in step (i) of a composition comprising the monomer of formula (I) and an acid-by product thereof. Support for this feature is found in the specification at page 10, lines 6-8 (based upon PCT/GB00/00780). Additional amendments include the simplification of claim language and consistent use of superscripts and/or subscripts for the recited variables.

Claim 2 has been amended to more clearly reflect that the acid is immobilized, support for which is found in claim 1.

Claim 3 has been amended to modify the spelling of immobilized.

Claim 4 has been amended to properly indicate dependence upon claim 1.

Claim 5 has been amended to simplify its language.

Claim 9 has been amended to more clearly recite that prior to the contacting step, the immobilized acid is contained.

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Claim 11 has been amended to modify the spelling of immobilized.

Claim 12 has been amended to correct an inadvertent word-processing error.

Claim 13 has been amended to conform to the language of newly amended claim 9 from which it depends.

Claim 14 has been amended to clarify the features of the recited extracting step as it pertains to claim 9 from which the claim depends.

Claim 15 has similarly been amended to more clearly reflect the step of polymerizing after the neutralizing step.

Claims 16 and 17 have been amended to conform to the language of claim 1 from which they each depend.

Claim 18 has been amended to more clearly reflect the step of incorporating the polymer formed in said polymerizing step into an ocular device. Support for this feature is found in the claim itself, as well as in the specification at page 12, lines 24-32.

Claims 19, 20, 21 have been amended to conform to the customary language used in U.S. practice.

Claim 23 Claim 23 recites the feature of a composition comprising the monomer of formula I and about 0.50 percent or less of cross-linker. Support for this feature is found in the specification at Figure 2.

Claim 24 recites formation of a reaction product P-C(O)-Q, support for which is found in the specification at page 12, lines 10-14.

Claim 25 recites essentially quantitative conversion of the compound of formula (II) to the resulting monomer. Support for this feature is found in the specification at page 12, lines 12-14.

Claim 26 recites a polymer product comprising 5% or less of a polymer formed by polymerization of a cross-linker. Support for this feature is found in the specification at page 16, line 15.

Claim 27 recites a neutralizing step that comprises contacting the composition of step (i) with immobilized alkali. Support for this feature is found on page 7, lines 5-6.

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Claim 28 recites an immobilized alkali which is an immobilized hydroxide.
Support for this feature is found on page 7 of the specification, lines 7-8.

Claim 29 recites removal by filtration of the immobilized acid. Support for this feature is found in the specification at page 18, line 5.

Claim 30 recites a particular starting material, product, by-product and linker, support for which is found in the specification at least at page 11, lines 15-20.

No new matter has been added to the claims by virtue of the amendments presented herein.

III. Rejection Under 35 U.S.C. §103

A. GROUNDS OF REJECTION

Claims 1-6, and 9-22 stand rejected under 35 U.S.C. §103(a) as unpatentable over Mancini et al., U.S. Patent No. 4,056,496 in view of Mitra et al., U.S. Patent No. 5,212,015, for the reasons stated in the Office action mailed March 15, 2006.

This rejection is respectfully traversed in view of the remarks that follow.

B. THE CLAIMED INVENTION

The claimed invention is directed to a process for preparing a polymerizable composition, where the resulting polymerizable composition comprises a polymerizable monomer and advantageously, small amounts of a cross-linker.

Specifically, the Applicant's claimed process, as embodied in independent claim 1, includes the following steps:

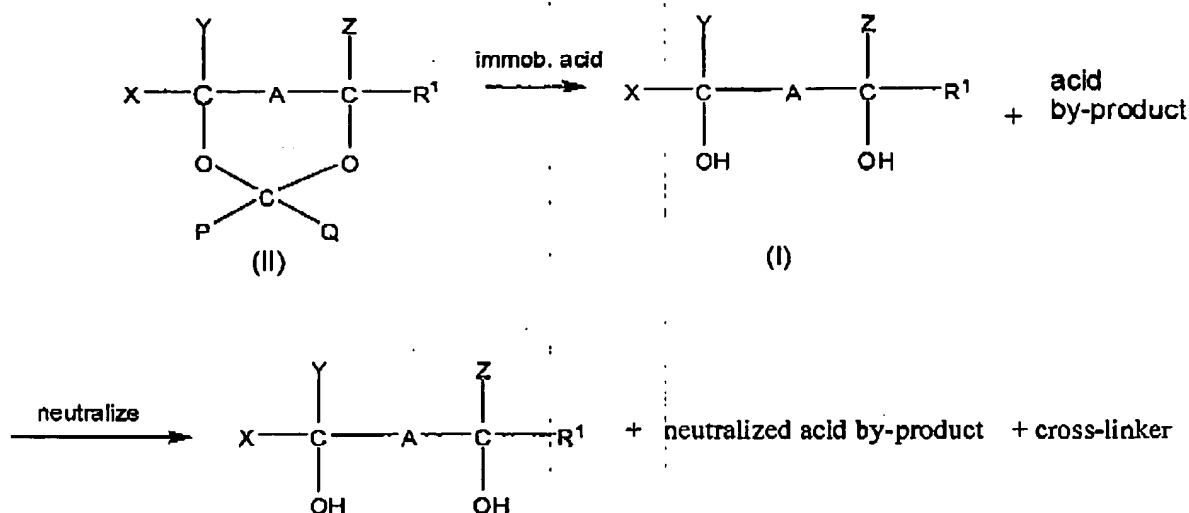
- (i) contacting a compound of formula (II) with an immobilized acid to form a composition comprising the monomer of formula (I) and an acid by-product thereof, and
- (II) neutralizing the composition of step (i) to thereby provide a composition comprising the monomer of step (i) and a cross-linker.

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The claimed process is shown generally in the reaction scheme below.



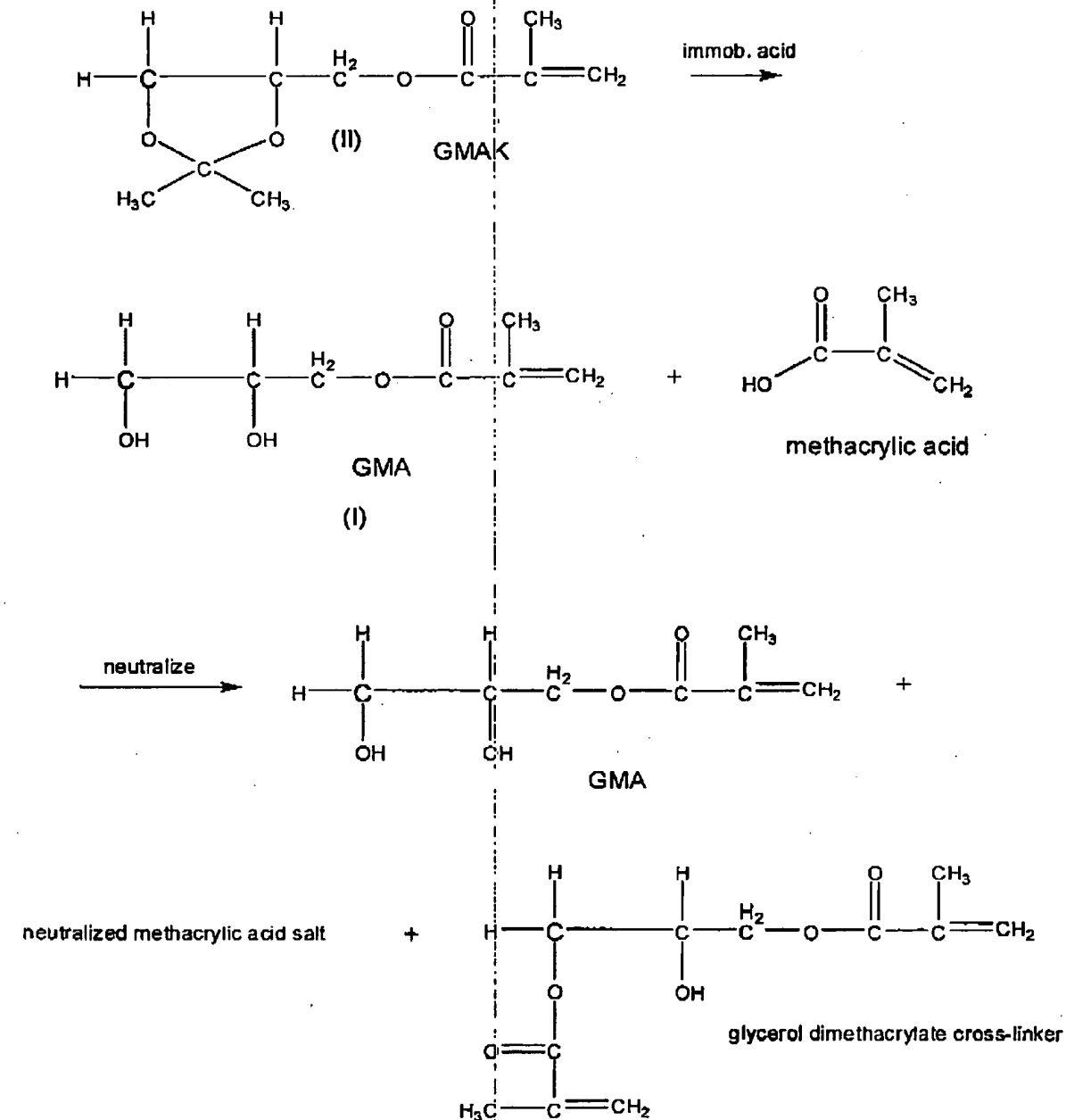
| Variable | Selected From |
|----------------|--|
| X | Hydrocarbyl*, H |
| Y | Hydrocarbyl*, H |
| Z | Hydrocarbyl*, H |
| P | Hydrocarbyl*, H |
| Q | Hydrocarbyl*, H |
| A | CH ₂ or absent |
| R ¹ | $ \begin{array}{c} \text{O} \quad \text{R}_2 \\ \quad \\ \text{---}(\text{CH}_2)\text{---O---C---C=CH}_2 \\ \text{or} \\ \text{O} \quad \text{R}_2 \\ \quad \\ \text{---}(\text{CH}_2)\text{---O---C---C---R}_3 \\ \quad \quad \text{H} \end{array} $ |
| R ₂ | H, -CH ₃ , -CH ₂ CH ₃ , -CH ₂ CH ₂ CH ₃ , -CH ₂ CH ₂ CH ₂ CH ₃ |
| R ₃ | Unsaturated C ₂₋₅ alkyl |

*a hydrocarbyl group comprises at least C and H, and may optionally comprise one or more suitable substituents.

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For the Examiner's ease of reference, and as recited in dependent claim 30, in one particular embodiment, the method of the invention comprises the following process steps:



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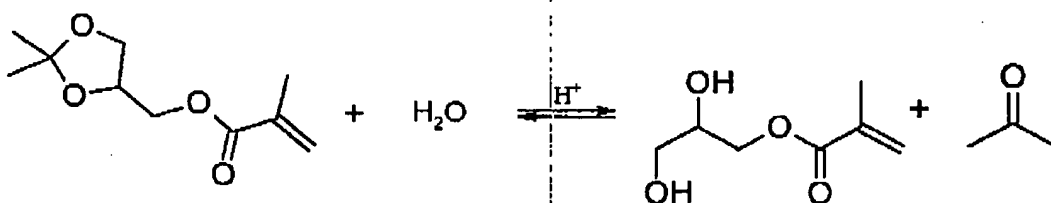
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In arriving at the claimed method, the inventors recognized the problem of consistently providing/obtaining polymerizable monomer compositions in a satisfactory pure form, i.e., having a very low and quantifiable level of impurities, especially cross-linker impurities. Such impurities are often detrimental to the final polymerized product, and can make such polymers unsuitable for use in products such as ocular devices. Moreover, polymers are very difficult to purify. The solution provided by the claimed invention is a process which utilizes a monomeric ketal starting material and an immobilized acid. The immobilized acid allows greater control of the reaction kinetics and side reactions, and results in a lower concentration of resulting acidic by-product(s), and following neutralization, of cross-linker. Moreover, the acid can be readily removed to allow facile isolation of the monomer product.

C. THE CITED ART

U.S. Patent No. 4,056,496 (Mancini). Mancini is directed to polymers and their resulting hydrogels, which are stated to be useful in soft contact lenses. Specifically, Mancini is directed to a polymer formed from a dihydroxyalkyl acrylate, an alkyl acrylate, and an epoxidized alkyl acrylate by a free radical polymerization in the substantial absence of solvent.

Mancini describes preparation of GMS as a starting material in Examples 1 and 2. Example 1 describes the following *solution phase* chemistry:



where the ketal, isopropylideneglyceryl methacrylate (GMAK), is reacted with *aqueous* sulfuric acid in the presence of hydroquinone. Excess sulfuric acid is neutralized by addition of barium hydroxide, and the resulting barium hydroxide salt is then removed by filtration.

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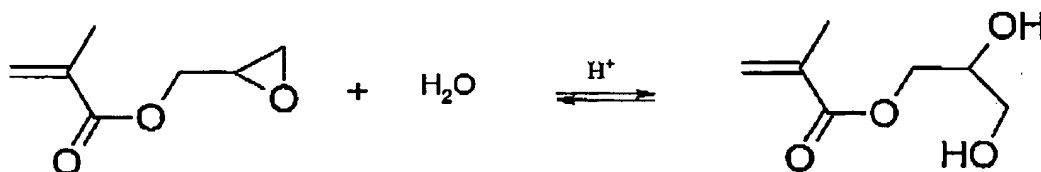
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First, nowhere does Mancini describe or even remotely suggest the use of an immobilized acid, nor the potential advantages thereof. Further, nowhere does Mancini teach, suggest, or recognize the formation of methacrylic acid in the above-reaction, nor the potential problems associated therewith, nor teach, suggest, or recognize the possibility of formation of *any* amount of a cross-linker during the neutralization step. The solution phase reaction of Mancini is completely different from a process standpoint than that embodied by the Applicant's claims. Moreover, nowhere does Mancini teach or recognize ANY problem associated with the processes described therein - such as acidifying a ketal monomer precursor under highly acidic conditions, which can lead to significant levels of degradation products and therefore resulting impurities, nor the formation of cross-linker in the subject reaction - which can be highly detrimental to the quality of the resulting monomer product, as well as the final polymer product formed via polymerization of the monomer.

Thus, nowhere does Mancini provide the slightest motivation to modify the teachings therein to arrive at the applicants claimed invention, since nowhere does Mancini recognize or suggest the slightest shortcoming with the methods described.

Indeed, rather than even remotely suggesting the use of an immobilized acid, Mancini suggests that a preferred method for preparing glyceryl methacrylate is as provided in Example 2, where GMA is prepared via solution phase acid hydrolysis of the epoxidized starting material, glycidyl methacrylate. This starting material has a structure that is completely different than the starting material, formula (II), recited in the instant claims. The reaction described in Example 2 is shown below:



The main impurity noted in the resulting product mixture is unreacted starting material, which Mancini suggests acts as a cross-linker (column 5, lines 23-24). This is completely different than a cross-linker that is formed as a reaction by-product as in the Applicant's claims. Moreover, since the subsequent polymerization method of Mancini

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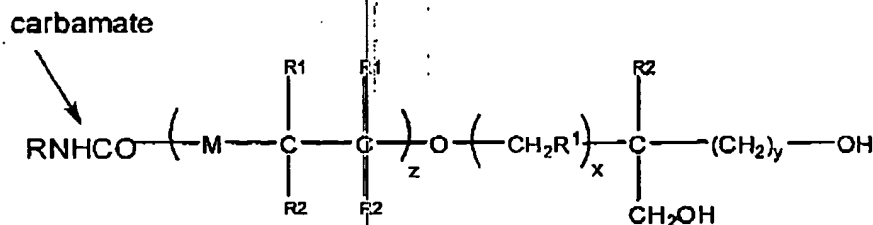
involves inclusion of an epoxized alkyl acrylate (believed to be a cross-linker as stated in column 5, lines 23-35), rather than removal of unreacted starting material (e.g., glycidyl methacrylate), Mancini actually suggests an amount of epoxidized acrylate in the monomer composition ranging from 0% to 30% by weight of the dihydroxy acrylate...most preferably from about 3.2 to about 7.5%. Thus, in no way does Mancini suggest a method that focuses on forming small amounts of cross-linker, in contrast, Mancini actually suggests just the opposite, i.e., that *an increase* in epoxized acrylate cross-linker may be required (column 5, lines 55-61).

In sum, in considering the teachings of Mancini as a whole, in no way does Mancini provide the slightest motivation for using an immobilized acid for any purpose, let alone for reducing side reactions and/or for reducing the amount of acidic and cross-linker reaction side-products.

U.S. Patent No. 5,212,015 (Mitra)

Mitra is directed to synthetic routes for providing single isomers of monocarbamate diols, as well as their polymerization. The products of Mitra are stated to be particularly useful in non-linear optics (NLO). Thus, Mitra is focused on providing pure, single isomers of carbamate diols. Mitra has absolutely nothing to do with compounds having the structures recited in the instant claims, nor with minimizing formation of either acid or cross-linker reaction by-products during formation of a product having the structure of Applicant's formula (I). Nor is Mitra focused on ophthalmic devices as recited in the instant claims. Rather, Mitra is focused on a problem that is completely unrelated to that addressed by the instant claims – Mitra is directed to the provision of *isomerically pure* monocarbamate diols.

Specifically, Mitra relates to preparing isomerically pure compounds having the general formula:



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These compounds are structurally dissimilar from the monomer of formula (I) recited in the Applicant's claims. Moreover, while Mitra is related to providing pure compounds, the focus of Mitra is the provision of *isomerically* pure compounds – not compounds having a greater degree of purity related to low levels of acidic and cross-linker impurities. Thus, the problems addressed by the Applicant's invention and those addressed by Mitra are completely unrelated.

Mitra describes that the above compounds can be prepared by acidification of the corresponding ketals. Mitra further describes that acidification can be carried out using an organic or non-oxidizing inorganic acid, or even using an ion exchange resin. However, Mitra provides absolutely no motivation or suggestion to modify the compounds that are the very focus of Mitra to arrive at a compound having the structure recited in the Applicant's claims. Nor does Mitra have anything to do with or recognize the problems addressed by the Applicant's invention. Indeed, neither of the references relied upon by the Examiner provides the slightest motivation for the combination made by the Examiner, nor for the modification of the teachings of the subject references to arrive at the claimed invention.

D. ANALYSIS

In determining whether a claimed invention is obvious, the following tenants must be adhered to:

- i. The claimed invention must be considered as a whole;
- ii. The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination or modification to arrive at the claimed invention; and
- iii. The references must be viewed without the benefit of hindsight afforded by the claimed invention or accompanying specification.

The claimed invention and the references relied upon by the Examiner are described in detail in the preceding sections.

The Examiner has suggested in the Office action mailed on March 15, 2006 that both Mancini and Mitra are related to the same endeavor of deacetalizing organic

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compounds (Office action, page 4, final paragraph). The undersigned respectfully submits that this is not the case. In considering each of the cited art references relied upon by the Examiner *in its entirety*, it can be seen that neither is directed to the deketalization of organic compounds. Rather, Mancini is directed to a process for forming a polymer by free radical polymerization of a dihydroxyalkyl acrylate, an alkyl acrylate, and an epoxidized acrylate, while Mitra is directed to a process for preparing single isomers of monocarbamate diols for use in non-linear optics.

In considering the teachings of the primary reference relied upon by the Examiner, Mancini, as a whole, it can be seen that:

- (i) Mancini fails to teach or suggest use of an immobilized acid;
- (ii) Mancini fails to recognize the possibility of formation of an acidic by-product during acidification of a ketal starting material to form a corresponding diol, and more importantly, the problems associated therewith;
- (iii) Mancini fails to recognize the possibility of formation of a cross-linker side-product during neutralization of an acidic product mixture resulting from acidification of a ketal starting material, and more importantly, the problems associated therewith, and the desirability of reducing the levels of such a cross-linker in the resulting monomer product.

In sum, Mancini provides absolutely *no motivation* for modifying the teachings therein to arrive at the Applicant's claimed method. That is to say, Mancini provides no motivation for using an immobilized acid – for any reason. The Examiner is reminded that *the references themselves* must suggest the desirability and thus the obviousness of making the combination or modification to arrive at the claimed invention – such a suggestion is clearly lacking in the references relied upon the Examiner.

In an effort to make up for the deficiencies of Mancini, the Examiner has relied upon the teachings of Mitra. However, Mitra is directed to the synthesis of monomers having a completely different structure from those embodied by the Applicant's claims. Moreover, Mitra is directed to a problem completely different from that of the Applicants – the problem of providing isomerically pure monocarbamate diols. And while Mitra does suggest that an immobilized acid may be used to convert a ketal of a compound having a structure completely different from those of the Applicant's claims to a diol –

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this has no bearing to Mancini. Nor does either reference provide even a remote suggestion of the desirability of applying the disparate teachings therein to arrive at the method of the claimed invention, for providing a monomer composition comprising low levels of cross linker or for any other purpose. Thus, it is submitted that the only motivation to combine and modify the references to arrive at the Applicant's claims is that provided by the Applicant's disclosure — which, as the Examiner knows, is impermissible under the tenants of 35 U.S.C. §103. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

In view of the above, it is submitted that the claims currently pending in the application are non-obvious over Mancini when considered in view of Mitra. Withdrawal of the rejection of the claims under 35 U.S.C. §103(a) is therefore respectfully requested.

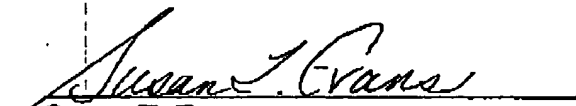
V. Conclusion

In view of the foregoing, the Applicant submits that all of the claims pending in the application patentably define over the cited art. A Notice of Allowance is therefore respectfully requested.

If a telephone conference would expedite the prosecution of the subject application, the Examiner is requested to call the undersigned at (650) 838-4406. The Commissioner is hereby authorized to charge any deficiency in fees or credit any overpayment to **Deposit Account No. 50-2207**.

Respectfully submitted,

Date: March 22, 2007


Susan T. Evans
Registration No. 38,443
on behalf of Applicant

PERKINS COIE LLP
101 Jefferson Drive
Menlo Park, CA 94025-1114
Tel: (650) 838-4406 / Fax: (650) 838-4350

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